Synthesis of 1,5-Benzodiazepine Nucleosides

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Summary: The phenolic β-diketones I prepared by modified Baker-Venkataraman rearrangement were converted to benzodiazepine derivatives II by treatment with o-phenylenediamine. Coupling of benzodiazepine derivatives II with acetobromo sugars in presence of mercuric cyanide and nitromethane gave acetylated sugar derivatives of benzodiazepines III. The nucleosides IV were obtained by the deacetylation of compounds III. Structures of all intermediates and final products were confirmed with the help of modern spectroscopic methods.

Introduction

The seven membered heterocycles have been the source of interest among the medical field because of the development of the several major drug entities. The benzodiazepines were introduced into clinical practice over 30 years ago. Since that time they have become the most frequently prescribed of all psychotropic drugs. These drugs are used as anxiolytics, hypnotics, anticonvulsants and muscle relaxant and their popularity is due, at least in some considerable part, to their large therapeutic ratio and essential lack of disturbing peripheral side effects [1].

1,5-benzodiazepines containing 1,2-benziso-xazole nucleus have shown antifungal activity [2]. Benzopyrano[4,3-b]-1,5-benzodiazepine has been described as sedative and analgesic [3]. 1,5-Benzodiazepines containing pyridyl and thienyl groups at 2 and 4 positions were known to have antimicrobial activity [4]. *N*-Acetyl, *N*-benzoyl and N,N-disubstituted aminoacetyl derivatives of 4-methyl-1*H*-tetrahydro-1,5-benzodiazepine-2-carbo-xylic acids were used as analgesic, antianxietic and anticonvulsant agents [5]. 2-(2′-Hydroxyphenyl)-4-aryl-1,5-benzodiazepines have been found to be CNS

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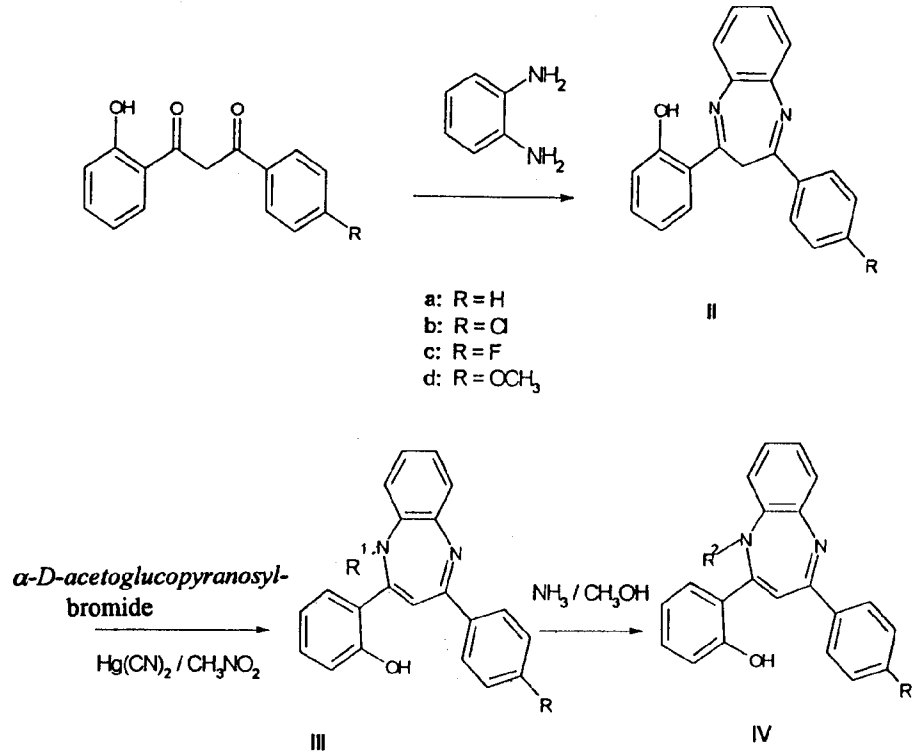

Fig. 1

active agents. These compounds have shown *in vitro* MAO (monoamino oxidase) activity and *in vivo* electrogenic and chemogenic anticonvulsant and hypnotic activities [6].

Result and Discussion

Keeping the potential biological activity of many of the benzodiazepine in mind, it was planned to synthesize benzodiazepine nucleosides **IV-A** to **IV-D**, by cyclocondensation of *o*-phenylenediamine with β-diketones (Figure 1). Phenolic β-diketones **I**, prepared according to a reported procedure [7], were subjected to cyclocondensation reaction with *o*-phenylenediamine under milder reaction conditions for a prolonged reaction time to give 2-(*o*-hydroxyphenyl)-4-(*p*-substituted phenyl)-1,5-benzodiazepines **IIa** to **IId** in 55-77 % yield. The IR spectra of these compounds showed a broad band in the region 3480 to 3580 cm^{-1} indicating the presence of a hydrogen bonded hydroxyl group. The ^{1}H-NMR data of these compounds is consistent with the data reported for 2,4-diphenyl-1,5-benzodiazepines [2,3]. The C-3 methylene protons resonated in the region of δ = 3.69 to 3.86 indicating that these compounds exist in diimine form. The phenolic protons, exchangeable with D_2O, appeared as singlets in the region δ = 14.39 to 14.56. In the ^{13}C-NMR spectra, C-3 resonated in the region between δ = 33.16 and 33.97 which indicated the diimine form of these compounds. A high field resonance of C-2 at δ = 161.43 to 163.30 indicated its attachment to the oxygen atom. In the mass spectra of **IIa** to **IId** the molecular ion peak is the most abundant peak

showing high stability of the molecular ion. The other major fragments were obtained due to the cleavage of H$^{\cdot}$, $RC_6H_4C{=}CH^{\cdot}$, $OC_6H_4C{=}CH^{\cdot}$, $C_6H_5O^{\cdot}$ and $R\text{-}C_6H_4^{\cdot}$ from the molecular ion.

Phenolic 1,5-benzodiazepine derivatives **IIa** to **IId** were coupled [8] with 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide in the presence of mercuric cyanide and nitro-methane to obtain 4''-substituted *N*-[tetra-*O*-acetyl-β-D-glucopyranosyl]-2-(*o*-hydroxyphenyl)-4-phenyl-1,5-benzodiazepines, **III-A** to **III-D**. In the IR spectra of these compounds sharp absorption bands due to acetyl groups were observed in the region 1720 to 1733 cm^{-1}. In the ^{1}H-NMR spectra of **III-A** to **III-D**, the protons of acetyl group resonated as singlets in the region of δ = 1.82 to 2.08. Methoxy protons in compound **III-D** resonated as singlet at δ = 3.78. The signals of C-3 protons were observed as singlets at δ = 7.26 to 7.28. The anomeric protons in all of these compounds resonated as doublets at δ = 5.31 to 5.34. The β-configuration of all the compounds was assigned by ^{1}H-NMR measurements. The C-1 sugar proton appeared as doublet with coupling constants of 6.0 to 6.6 Hz, which is a clear indication of the diaxial orientation of C-1 and C-2 sugar protons. The C-4 sugar protons in all of these compounds resonated as doublet of doublets in the region δ = 4.37 to 4.39 while C-3 and C-2 protons appeared as multiplets in the region δ = 5.18 to 5.19 and δ = 3.90 to 3.91, respectively. Aromatic protons appeared in the region of δ = 6.77 to 7.85. Some important ^{1}H-NMR absorptions of these compounds are tabulated in table 1. In the ^{13}C-NMR spectra of **III-A** to **III-D** the methyl carbons of acetyl groups resonated in the region between δ = 20.41 and 20.57 while the carbonyl carbons of acetyl groups appeared at δ = 72.13 to 72.22. The anomeric carbons resonated in the region of δ = 99.64 to 99.93 indicating their direct linkage with nitrogen atoms of heterocyclic moiety. The EI mass spectra of **III-A** to **III-D** showed very weak molecular ion peaks. However, the field desorption mass spectra showed molecular ion peaks with 100 % intensity.

The deacetylation of **III-A** to **III-D** was successfully carried out in methanolic ammonia to give nucleosides **IV-A** to **IV-D** in 51-71 % yield. In IR spectra of these compounds, free -OH stretching bands were observed in the region 3340 to 3350 cm^{-1}. No signal was observed due to the carbonyl group. In the ^{1}H-NMR spectra of **IV-A** to **IV-D**, doublets were observed due to anomeric protons which resonated in the region δ = 4.82 to 4.86 with a coupling constant of 6.75 to 8.50 Hz giving a clear indication of the diaxial orientation of C-1 and C-2 sugar protons, hence confirming the β-configuration in these compounds. In **IV-C**, C-6 sugar protons resonated as broad singlets at δ = 3.64 and at δ = 3.85, while in all other compounds they resonated as multiplets in the region of δ = 3.61 to 3.76. The C-2 protons of sugars in **IV-A**, **IV-B** and **IV-D** resonated as broad singlets at δ = 3.31 to 3.34 while in **IV-C** it resonated at δ = 3.46 as a singlet. The protons at C-3 in **IV-A** and **IV-B** resonated as multiplets in the region of δ = 3.62 to 3.72 and 3.61 to 3.72, respectively, while in compound **IV-C** it appeared as broad singlet at δ = 3.64. In compound **IV-D**, the C-3 sugar proton was observed as singlet at δ = 3.60. In all these compounds, the -OH protons resonated as broad singlets at δ = 5.49 to 5.90. In compound **IV-D**, a singlet due to three methoxy protons was observed at δ = 3.70. Aromatic protons resonated in the region of δ = 6.77 to 7.84. ^{1}H-NMR absorptions of sugar protons in these compounds are represented in table 2. The molar masses of compounds **IV-A** to **IV-D** were confirmed by field desorption mass spectra.

Table 1 : Some important ^{1}H-NMR data of compounds III (a-d)

Sr. No.	Compound	H-3	Sugar protons 1	2	3	4	5	6
1	IIIa	7.26	5.31	3.90	5.18	4.38	4.18	5.18(m)
		s	d, J = 6.5 Hz	m	m	dd	d	5.29(s)
2	IIIb	7.26	5.34	3.90	5.18	4.39	4.19	5.18(m)
		s	d, J = 6 Hz	m	m	dd	m	5.30(s)
3	IIIc	7.28	5.33	3.91	5.19	4.38	4.18	5.19(m)
		s	d, J = 6 Hz	m	m	dd	d	5.29(s)
4	IIId	7.28	5.32	3.90	5.19	4.37	4.17	5.19(m)
		s	d, J = 6 Hz	m	m	dd	d	5.29(s)

Table 2 : ^{1}H-NMR data of sugar protons in compounds IV (a-d)

Sr. No.	Compound	protons 1	2	3	4	5	6
1	IVa	4.83 (d) J = 6.75 Hz	3.31 b.s.	3.62-3.74 m	3.49 t	3.38 b.s.	3.62-3.74 (m)
2	IVb	4.86 (d) J = 7.05 Hz	3.32 b.s.	3.61-3.72 m	3.61-3.72 m	3.49 t	3.61-3.72 (m)
3	IVc	4.85 (d) J = 8.5 Hz	3.46 s	3.64 b.s.	3.64 b.s.	3.64 b.s.	3.64(b.s.) 3.85(b.s.)
4	IVd	4.82 (d) J = 7.3 Hz	3.34 b.s.	3.60 s	3.63 b.s	3.52 t	3.64-3.76 (m)

Experimental

General Procedure for Cyclocondensation of 1,3-Diketones with Phenylenediamine :

1-(2′-hydroxyphenyl)-3-(4′-substituted phenyl)-propane-1,3-dione (0.01 mole) was dissolved in toluene, glacial acetic acid (5 ml) was added followed by *o*-phenylenediamine (0.01 mole) and the mixture was refluxed for six hours. Solvent was removed under reduced pressure to dryness and the mixture was treated with small quantity of methanol. Precipitates obtained were again washed with small amount of methanol and recrystallized from isopropanol.

2-(2′-Hydroxyphenyl)-4-phenyl-1,5-benzodiazepine (IIa) :

m. p. = 183-184 °C. Yield = 68 %. IR (ν_{max}, KBr, cm^{-1}) : 3064, 2362, 1617, 1596, 1572, 1449, 1311, 759. ^{1}H-NMR ($CDCl_3$, δ-values) : 3.85 (s, broad, 2H, H-3), 6.94 (t, 1H), 7.08 (d, 1H, J = 8.40 Hz), 7.44 (m, 3H), 7.54 (m, 3H), 7.65 (dd, 1H, J = 7.75 Hz), 7.72 (d, 1H, J = 7.80 Hz), 7.87 (dd, 1H, J = 8.05 Hz), 8.10 (m, 2H), 14.55 (s, 1H, -OH, exchangeable with D_2O). ^{13}C-NMR ($CDCl_3$, δ-values) : 155.17 (C-2), 33.33 (C-3), 158.48 (C-4), 137.23 (C-5a), 136.80 (C-9a), 125.81 (C-6), 127.89 (C-7), 128.75 (C-8), 126.28 (C-9), 117.91 (C-1′), 162.53 (C-2′), 118.44 (C-3′), 133.51 (C-4′), 118.56 (C-5′), 130.95 (C-6′), 141.62 (C-1″), 128.82 (C-2″ and C-6″), 128.28 (C-3″ and C-5″), 128.99 (C-4″). Mass m/z (%) : 312 ($M^{+\cdot}$ and 100 %), 311 (88), 297 (61), 283 (22), 235 (44), 219 (10), 210 (10), 194 (42), 193 (20), 182 (9), 181 (18), 91 (7), 90 (9).

2-(2′-Hydroxyphenyl)-4-(4′-chlorophenyl)-1,5-benzodiazepine (IIb) :

m. p. = 229-232 °C. Yield = 72 %. IR (ν_{max}, KBr, cm^{-1}) : 3088, 1593, 1563, 1455, 1443, 1401, 1332, 768. ^{1}H-NMR ($CDCl_3$, δ-values) : 3.86 (s, 2H, H-3), 6.88 (t, 1H), 6.99 (d, 1H, J = 8.32 Hz), 7.33-7.47 (m, 4H), 7.52-7.63 (m, 2H), 7.76 (dd, 1H, J = 8.07 Hz), 7.94-7.99 (m, 3H), 14.39 (s, 1H, -OH, exchangeable with D_2O). ^{13}C-NMR ($CDCl_3$, δ-values) : 154.12 (C-2), 33.21 (C-3), 155.39 (C-4), 136.21 (C-5a), 136.01 (C-9a), 125.42 (C-6), 127.35 (C-7), 128.17 (C-8), 125.97 (C-9), 118.02 (C-1′), 161.43 (C-2′), 118.40 (C-3′), 132.43 (C-4′), 119.09 (C-5′), 130.12 (C-6′), 139.43 (C-1″), 133.44 (C-2″ and C-6″), 129.34 (C-3″ and C-5″), 138.60 (C-4″). Mass m/z (%) : 346 ($M^{+\cdot}$ and 100 %), 345 (84), 331 (62), 317 (23), 253 (7), 228 (18), 227 (18), 210 (9), 207 (11), 194 (7), 182 (9), 181 (10), 91 (9), 90 (12).

2-(2′-Hydroxyphenyl)-4-(4′-fluorophenyl)-1,5-benzodiazepine (IIc) :

m. p. = 201 °C. Yield = 55 %. IR (ν_{max}, KBr, cm^{-1}) : 3450, 1602, 1575, 1506, 1455, 1443, 1335, 756. ^{1}H-NMR ($CDCl_3$, δ-values) : 3.74 (s, broad, 2H, H-3), 6.87 (t, 1H), 6.99 (d, 1H, J = 8.30 Hz), 7.14 (t, 1H), 7.36 (m, 2H), 7.52-7.62 (m, 3H), 7.76 (d, 1H, J = 8.04 Hz), 8.03 (m, 3H), 14.43 (s, 1H, -OH, exchangeable with D_2O). ^{13}C-NMR ($CDCl_3$, δ-values) : 153.97 (C-2), 33.34 (C-3), 156.21 (C-4), 126.42 (C-5a), 125.95 (C-9a), 127.96 (C-6), 130.48 (C-7), 130.62 (C-8), 128.05 (C-9), 118.61 (C-1′), 163.30 (C-2′), 116.08 (C-3′), 130.62 (C-4′), 118.67 (C-5′), 130.48 (C-6′), 138.72 (C-1″), 128.21 (C-2″ and C-6″), 115.73 (C-3″ and C-5″), 167.39 (C-4″). Mass m/z (%) : 330 ($M^{+\cdot}$ and 100 %), 329 (85), 315 (50), 301 (25), 237 (7), 235 (17), 212 (36), 210 (7), 194 (6), 182 (6), 181 (13), 91 (6), 90 (12).

2-(2′-Hydroxyphenyl)-4-(4′-methoxyphenyl)-1,5-benzodiazepine (IId) :

m. p. = 208-210 °C. Yield = 63 %. IR (ν_{max}, KBr, cm^{-1}) : 3440, 1605, 1563, 1443, 1326, 753. ^{1}H-NMR ($CDCl_3$, δ-values) : 3.69 (s, broad, 2H, H-3),

3.84 (s, 3H, -OCH_3), 6.83-7.02 (m, 3H), 7.29-7.43 (m, 3H), 7.51-7.63 (m, 2H), 7.79 (dd, 1H, J = 8.08 Hz), 7.97-8.04 (m, 2H), 14.56 (s, 1H, -OH, exchangeable with D_2O). ^{13}C-NMR ($CDCl_3$, δ-values) : 154.51 (C-2), 33.16 (C-3), 158.51 (C-4), 129.51 (C-5a), 137.16 (C-9a), 125.48 (C-6), 127.97 (C-7), 128.32 (C-8), 126.30 (C-9), 118.04 (C-1'), 161.99 (C-2'), 118.49 (C-3'), 133.48 (C-4'), 118.57 (C-5'), 128.97 (C-6'), 141.89 (C-1''), 130.21 (C-2'' and C-6''), 114.15 (C-3'' and C-5''), 162.60 (C-4''), 55.44 (OCH_3). Mass m/z (%) : 342 (M^+ and 100 %), 341 (60), 327 (52), 313 (24), 249 (9), 235 (20), 224 (32), 223 (14), 210 (6), 207 (13), 194 (8), 182 (10), 181 (15), 91 (8), 90 (12).

General Procedure for the synthesis of N-*Glycosides* [8]:

To a mixture of 2.0 mmoles of acetobromosugar (2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide), 2.0 mmoles of mercuric cyanide and 2.0 g of anhydrous calcium sulfate (or molecular sieves) in 30 ml of dry nitromethane, was added 1 mmole of the 1,5-diazepine. The mixture was refluxed for 2-4 hours. After this, it was filtered while still hot in order to remove an insoluble residue which was washed with more hot nitromethane, and the filtrate was evaporated to dryness *in vacuo*. The product obtained was treated with dichloromethane and filtered to separate the solid (a complex formed by mercuric halide and the corresponding heterocycles). The dichloromethane extract was washed with 30 % aqueous potassium iodide, water and then dried over anhydrous sodium sulfate. Finally, the product obtained after removing the solvent was purified with the help of column chromatography using silica gel as adsorbent and benzene/acetone mixture as eluent.

N-[Tetra-O-acetyl-β-D-glucopyranosyl]-2-(o-hydroxyphenyl)-4-phenyl-1 5-benzodiazepine (III-A) :

m. p. = 137.0-138.3 °C. Yield = 52 %. ^{1}H-NMR ($CDCl_3$, δ-values) : 1.82 (s, 3H, CH_3CO), 1.98 (s, 6H, 2 X CH_3CO-), 2.05 (s, 3H, CH_3CO-), 3.90 (m, 1H), 4.18 (d, 1H), 4.38 (dd, 1H), 5.18 (m, 2H), 5.29 (s, 1H), 5.31 (d, 1H, J = 6.50 Hz, H-1, sugar), 7.03 (t, 1H, Ar-H), 7.19 (dd, 1H, Ar-H), 7.26 (s, 1H, H-3), 7.32 (m, 1H, Ar-H), 7.58 (m, 1H, Ar-H), 7.79 (dd, 2H, Ar-H). ^{13}C-NMR ($CDCl_3$, δ-values) : 20.43 (-$COCH_3$), 20.57 (3 X -$COCH_3$), 61.78 (C-6, sugar), 68.13 (C-5, sugar), 70.94 (C-2, sugar), 72.21 (C-3, sugar), 72.63 (C-4, sugar), 99.86 (C-1,sugar), 124.16 (C-3'), 128.51 (C-2' and C-6'), 128.68 (C-2'' and C-3''), 129.97 (C-1'), 130.36 (C-4''), 131.61 (C-6'), 131.72 (C-4'), 137.59 (C-5a), 140.31 (C-9a), 154.84 (C-2), 155.45 (C-4), 155.84 (C-2'), 169.20 (CO), 169.37 (CO), 170.13 (CO), 170.49 (CO).Mass m/z (%) : 642 (M^+ and 4), 582 (3), 522 (5), 462 (9), 419 (5), 330 (7), 311 (21), 271 (4), 235 (7), 211 (7), 194 (32), 169 (100 %), 145 (8), 127 (27), 109 (92), 97 (13), 71 (14).

N-[Tetra-O-acetyl-β-D-glucopyranosyl]-2-(o-hydroxyphenyl)-4-(p-chlorophenyl)-1,5-benzodiazepine (III-B) :

m. p. = 131.5 - 132 °C. Yield = 48 %. ^{1}H-NMR ($CDCl_3$, δ-values): 1.84 (s, 3H, CH_3CO-), 2.00 (s, 3H, CH_3CO-), 2.03 (s, 3H, CH_3CO-), 2.07 (s, 3H, CH_3CO-), 3.90 (m, 1H), 4.19 (m, 1H), 4.39 (dd, 1H), 5.18 (m, 2H), 5.30 (s, 1H), 5.34 (d, 1H, J = 6.0 Hz, H-1, sugar), 7.04 (t, 1H, Ar-H), 7.19 (m, 1H, Ar-H), 7.26 (s, 1H, H-3), 7.30-7.44 (m, 6H, Ar-H), 7.58 (t, 2H, Ar-H), 7.78 (d, 2H, Ar-H). ^{13}C-NMR ($CDCl_3$, δ-values) : 20.42 (-$COCH_3$), 20.53 (3 X -$COCH_3$), 61.69 (C-6, sugar), 68.05 (C-5, sugar), 70.33 (C-2, sugar), 72.21 (C-3, sugar), 72.51 (C-4, sugar), 99.93 (C-3), 124.19 (C-3'), 125.40 (C-5'), 128.41 (C-8), 128.44 (C-6), 128.47 (C-7), 128.77 (C-3'' and C-5''), 129.29 (C-2'' and C-6''), 131.72 (C-6'), 135.96 (C-5a), 136.68 (C-4''), 139.78 (C-1''), 140.85 (C-9a), 153.25 (C-2), 155.39 (C-4), 155.39 (C-2'), 169.17 (-CO-), 169.34 (-CO-), 170.07(-CO-), 170.42(-CO-). Mass m/z (%) : 675 (M^+ and 4), 617 (3), 556 (6), 496 (7), 477 (4), 388 (1), 345 (10), 330 (14), 307 (1), 228 (13), 217 (4), 211 (6), 169 (100%), 145 (8), 127 (23), 109 (13), 85 (12), 71 (19).

N-[Tetra-O-acetyl-β-D-glucopyranosyl]-2-(o-hydroxyphenyl)-4-(p-fluorophenyl)-1,5-benzodiazepine (III-C) :

m. p. = 120.0 - 120.9 °C. Yield = 38.5 %. ^{1}H-NMR ($CDCl_3$, δ-values) : 1.84 (s, 3H, CH_3CO-), 1.98 (s, 3H, CH_3CO-), 2.04 (s, 3H, CH_3CO-), 2.08 (s, 3H, CH_3CO-), 3.91 (m, 1H), 4.18 (d, 1H), 4.38 (dd, 1H), 5.19 (m, 2H), 5.29 (s, 1H), 5.33 (d, 1H, J = 6.0 Hz, H-1, sugar), 6.77-7.07 (m, 4H, Ar-H), 7.17 (dd, 2H, Ar-H), 7.28 (s, 1H, H-3), 7.31-7.44 (m, 2H, Ar-H), 7.53-7.60 (m, 2H, Ar-H), 7.68-7.85 (d, 2H,

Ar-H).^{13}C-NMR ($CDCl_3$, δ-values):20.43 (-$COCH_3$), 20.55 (3 X -$COCH_3$), 61.71 (C-6, sugar), 68.07 (C-5, sugar), 70.90 (C-2, sugar), 72.22 (C-3, sugar), 72.54 (C-4, sugar), 99.90 (C-1, sugar), 115.44 (C-3'' and C-5''), 124.19 (C-5'), 125.27 (C-9), 125.74 (C-6), 129.81 (C-1'), 131.70 (C-2'' and C-6''), 133.66 (C-5a), 140.15 (C-9a), 153.38 (C-2), 155.43 (C-4), 155.51 (C-2'), 165.46 (C-4''), 169.19 (-CO-), 169.37 (-CO-), 170.09 (-CO-), 170.44 (-CO-). Mass m/z (%) : 661 (M^+ and 3), 601 (4), 540 (6), 480 (8), 437 (4), 359 (1), 330 (17), 314 (2), 271 (4), 235 (5), 212 (17), 187 (2), 169 (100), 145 (8), 127 (24), 109 (76), 85 (23), 71 (53).

N-[Tetra-O-acetyl-β-D-glucopyranosyl]-2-(o-hydroxyphenyl)-4-(p-methoxyphenyl)-1,5-benzodiazepine (III-D) :

m. p. = 145-146 °C. Yield = 43.5 %. ^{1}H-NMR ($CDCl_3$, δ-values) : 1.85 (s, 3H, CH_3CO-), 1.99 (s, 3H, CH_3CO-), 2.06 (s, 3H, CH_3CO-), 3.78 (s, 3H, -OCH_3), 3.90 (m, 1H), 4.17 (d, 1H, 4.37 (dd, 1H), 5.19 (m, 2H), 5.29 (s, 1H), 5.32 (d, 1H, J = 6.0 Hz, H-1, sugar), 6.82 (d, 2H, Ar-H), 7.02 (t, 1H, Ar-H), 7.13 (d, 1H), 7.21 (d, 1H), 7.28 (s, 1H, H-3), 7.29-7.43 (m, 3H), 7.55 (m, 2H), 7.79 (d, 2H, Ar-H). ^{13}C-NMR ($CDCl_3$, δ-values) : 20.41 (-$COCH_3$), 20.53 (3 x -$COCH_3$), 55.27 (-OCH_3), 61.74 (C-6, sugar), 68.09 (C-5, sugar), 70.33 (C-2, sugar), 72.13 (C-3, sugar), 72.58 (C-4, sugar), 99.64 (C-1, sugar), 113.95 (C-3'' and C-5''), 124.15 (C-3'), 124.79 (C-5'), 125.80 (C-9), 129.42 (C-8), 129.74 (C-2'' and C-6''), 130.03 (C-1'), 131.47 (C-6'), 131.63 (C-4'), 140.48 (C-5a), 140.51 (C-9a), 154.03 (C-2), 155.39 (C-4), 155.91 (C-2'), 161.43 (C-4'), 168.14 (-CO-), 169.32 (-CO-), 170.08 (-CO-), 170.43 (-CO-). Mass m/z (%) : 671 (M^+ and 3), 630 (1), 613 (8), 569 (1), 552 (8), 510 (1), 492 (18), 448 (6), 371 (2), 341 (29), 326 (5), 297 (3), 271 (3), 247 (3), 224 (55), 209 (4), 169 (100), 145 (8), 127 (27), 109 (83), 97 (10), 71 (12).

General Procedure for Deacetylation :

One mmol. of the acetylated nucleoside was dissolved in 100 ml of dry methanol and a fairly rapid stream of dry ammonia was passed into the solution for two hours. The solution was kept at 0-5 °C for 20 hours and filtered. The solution was then concentrated to a syrup under reduced pressure at room temperature. The syrup was dissolved in methanol and again evaporated to a small volume. Purification was carried out by column chromatography using silica gel as adsorbent and ethylacetate as eluent.

N(β-D-Glucopyranosyl)-2-(o-hydroxyphenyl)-4-phenyl-1,5-benzodiazepine (IV-A) :

m. p. = 179.5-180.7 °C. Yield = 68 %. UV[λ_{max} (ε)nm] : 253.8 (18763.02), 225.20 (16414.09). IR (ν_{max}, KBr, cm^{-1}) : 3340, 2910, 1580, 760. ^{1}H-NMR ($CDCl_3$, δ-values) : 3.31 (bs, 1H, H-2, sugar), 3.38 (bs, 1H, H-5, sugar), 3.49 (t, 1H, H-4, sugar), 3.62-3.74 (m, 3H, H-3, sugar and H-6, sugar), 4.83 (d, 1H, J = 6.75 Hz, H-1, sugar), 5.74 (bs, 2H, -OH), 5.78 (bs, 2H, -OH), 6.92 (t, 1H, Ar-H), 7.13 (d, 1H, J = 8.05 Hz, Ar-H), 7.17-7.33 (m, 8H, Ar-H), 7.46 (d, 1H, J = 7.5 Hz, Ar-H), 7.50 (d, 1H, J = 6.8 Hz, Ar-H), 7.77 (d, 2H, J = 7.1 Hz, Ar-H). Mass F. D. : 474 (100 %).

N(β-D-Glucopyranosyl)-2-(o-hydroxyphenyl)-4-(p-chlorophenyl)-1,5-benzodiazepine (IV-B):

m. p. = 193-195 °C. Yield = 71 %. UV[λ_{max} (ε)nm] : 259 (10225.9), 224.1 (7873.0). IR (ν_{max}, KBr, cm^{-1}) : 3350, 2900, 1560, 760. ^{1}H-NMR ($CDCl_3$, δ-values) : 3.32 (bs, 1H, H-2, sugar), 3.49 (t, 1H, H-5, sugar), 3.61-3.72 (m, 4H, H-3, sugar, H-4,sugar and H-6, sugar), 4.86 (d, 1H, J = 7.05 Hz, H-1, sugar), 5.81 (bs, 2H, -OH), 5.90 (bs, 2H, -OH), 6.93 (t, 1H, Ar-H), 7.135 (d, 1H, J = 8.2 Hz, Ar-H), 7.18-7.25 (m, 4H, Ar-H and H-3), 7.30 (t, 1H, Ar-H), 7.44-7.49 (q, 3H, Ar-H), 7.22 (d, 2H, J = 8.5 Hz, Ar-H). Mass F. D. : 508.5 (100 %).

N(β-D-Glucopyranosyl)-2-(o-hydroxyphenyl)-4-(p-fluorophenyl)-1,5-benzodiazepine (IV-C) :

m.p. = 164-165 °C. Yield = 58.0 %. IR (ν_{max}, KBr, cm^{-1}) : 3350, 2929, 1580, 760. ^{1}H-NMR ($CDCl_3$, δ-values) : 3.46 (s, 1H, H-2'), 3.64 (bs, 4H, H-3,4,5 and 6 sugar protons), 3.85 (bs, 1H, H-6, sugar), 4.85 (d, 1H, J = 8.5 Hz, H-1, sugar), 5.49 (bs, 2H, -OH), 5.56 (bs, 2H, -OH), 7.00 (t, 1H, Ar-H), 7.09-7.14 (m, 4H, Ar-H), 7.24 (s, 1H, H-3), 7.28 (t, 1H, Ar-H), 7.51 (m, 3H, Ar-H), 7.56 (d, 1H, J = 8.8 Hz, Ar-H), 7.84 (d, 2H, J = 8.15 Hz, Ar-H). Mass F. D. : 492 (100 %).

N(β-D-Glucopyranosyl)-2-(o-hydroxyphenyl)-4-(p-methoxyphenyl)-1,5-benzodiazepine (IV-D) :

m. p. = 201-203 °C. Yield = 73 %. UV[λ_{max} (ε)nm] : 288.2 (31096.8), 225.2 (30266.8). IR (ν_{max}, KBr, cm^{-1}) : 3350, 2911, 1563, 762. ^{1}H-NMR

($CDCl_3$, δ-values) : 3.34 (bs, 1H, H-2, sugar), 3.52 (t, 1H, H-5, sugar), 3.64 (bs, 1H, H-4, sugar), 3.60 (s, 1H, H-3, sugar), 3.64-3.76 (m, 5H, $-OCH_3$ and H-6, sugar), 4.82 (d, 1H, J = 7.3 Hz, H-1, sugar), 5.54 (bs, 4H, -OH), 6.77 (d, 2H, J = 8.7 Hz, Ar-H), 6.96 (bs, 1H, Ar-H), 7.14 (d, 1H, J = 8.3 Hz, Ar-H), 7.18 (t, 1H, Ar-H), 7.21-7.35 (m, 4H, Ar-H and H-3), 7.47 (q, 2H, Ar-H), 7.77 (d, 2H, J = 8.8 Hz, Ar-H). Mass F. D. : 504 (100 %).

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